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Original Articles

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Defining urine output criterion for acute kidney injury in critically ill patients

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Abstract

Background. The widespread use of RIFLE and AKIN classification systems for acute kidney injury (AKI) diagnosis and staging has established the association between AKI severity and adverse outcomes. However, as a result of the difficulties in measuring and recording the urine output every hour, a few prospective studies have validated the urine output criterion as stated in these classification systems. We assessed hourly urine output in ICU patients using an automated and accurate device to determine if changes in urine flow and volume could be a sensitive marker of AKI. Additionally, we assessed various definitions of oliguria to determine whether measurement of urine output using a fixed 6-h interval that matches nurses' shifts would be equivalent to the current standard for AKI diagnosis and staging.

Methods. Hourly urine output was recorded continuously using a digital monitor in a medical ICU. Serum creatinine measurements were done at least once per 24 h. We assessed changes in urine output by four different definitions of oliguria. Patients with no AKI by either criterion were compared with patients diagnosed exclusively by the urine output criterion, exclusively by serum creatinine criterion and by both criteria.

Results. Fifty-five percent of patients had an episode of oliguria during the ICU stay. There was no significant difference assessing urine output every hour or the total urine volume in a 6-h period for the detection of episodes of oliguria. Twenty-one patients (28%) were diagnosed as AKI using the serum creatinine criterion, whereas additional 24 (32%) were identified by the urine output criterion.

Conclusions. Episodes of oliguria occur frequently in ICU patients and identify a higher percentage of AKI patients compared to serum creatinine criterion. Alterations in urine flow may be a sensitive marker of renal dysfunction and need to be validated in larger cohorts.

Keywords: acute kidney injury; clinical epidemiology; critically ill; oliguria; urine output

Introduction

It is now well recognized that, in hospitalized patients, small changes in serum creatinine are associated with significantly higher morbidity, mortality and costs, particularly in the intensive care unit (ICU) population. Several studies have already validated the RIFLE and AKIN classification system [1–3], demonstrating that patient outcome is progressively worse with the severity of acute kidney injury (AKI). Urine output is included as a criterion for diagnosing AKI in the RIFLE and AKIN classification systems; however, a few prospective studies have validated this criterion [4,5].

Although it is recognized that hydration status, use of diuretics and haemodynamic status will influence urine volume and that severe AKI can occur with normal urine output, the ADQI group decided that the use of decline in urine flow might be a sensitive marker of renal dysfunction. The ADQI group also acknowledged that the pattern of change of urine flow can be detected earlier with more frequent observations (every hour). Unfortunately, in the ICU, the actual methods for measurement of urine output are not standardized. The traditional way of monitoring urine output is by visual readings of the amount of urine accumulated in a urine metre, a process that is often inaccurate. Measurement of urine output every hour is time-consuming for the nursing staff, as the urine metres require manipulation, visual assessment and manual data recording. In most ICUs, the nurses empty the collection bag every 6 h, making the applicability of the urine output as stated by AKIN and RIFLE a challenge. These difficulties in measuring, monitoring and accurately recording urine output have resulted in lack of a standardized approach to assess changes in urine output and hampered the identification of episodes of oliguria.

We hypothesized that, using an accurate device to measure hourly urine output, changes in urine flow and volume would be a sensitive marker of AKI. Additionally, we assessed the practicality of implementing various definitions of oliguria to determine whether measurement of urine

output using a fixed 6-h interval that matches nurses' shifts is equivalent to the current standard for AKI diagnosis and staging.

Materials and methods

We prospectively studied patients admitted to a medical ICU at the University of California San Diego Medical Center. During a 2-month period, all patients older than 18 who had indwelling urinary catheters were eligible for enrolment. Patients with known end-stage renal disease or receiving renal replacement therapy were excluded. Urine flow was measured by a digital continuous urine metre (URINFO®, FlowSense Medical Ltd., Israel) [6]. The device uses an infrared light to detect urine flow drop-by-drop, providing an hourly accurate measurement of the urine flow. The study was approved by the Institutional Review Board, and a waiver of individual authorization for use of Protected Health Information was granted as stipulated by the Health Insurance Portability and Accountability Act rules.

Demographic data, co-morbidities, clinical history and laboratory studies were recorded from the day of ICU admission until ICU discharge. Serum creatinine measurements were done at least once per 24 h. We applied the AKIN classification system to define AKI by serum creatinine (creatinine increases ≥0.3 mg/dL or ≥50% above the reference value within 48 h). We considered the first serum creatinine measured at ICU admission as the reference serum creatinine. We computed daily and cumulative fluid balance for each patient; however, we did not record details of the type and duration of fluid administration, use of diuretics and other medications, or information on severity of illness.

We classified patients using four different definitions of oliguria based on the time interval for evaluation (Table 1). The first UO definition (UO1) is the actual AKIN stage 1 urine output criterion, which requires six consecutive hours with a urine volume ≤0.5 mL/kg. UO2 and UO3 assess the total volume of urine over a 6-h interval and consider oliguria if this volume is ≤3 mL/kg. In UO3, the 6-h interval is fixed and corresponds to the nurse's shift, from 6AM to 12PM and so forth. UO4 corresponds to the AKIN stage 2 time interval, assessing the urine output in a 12-h period, and defines oliguria using the total urine volume during this period (≤6 mL/kg). We assessed the sensitivity and specificity of each definition of oliguria using the serum creatinine AKIN criterion as the gold standard. The extent of oliguria over the time course of ICU stay was evaluated by the number of episodes of oliguria, with each episode representing the defined criteria for the UO definition, e.g. for UO3, combined period of six fixed block hours of <3 mL/kg = one episode. An additional measure was the total duration of oliguria during the ICU stay, reflecting the cumulative sum of hours the patient had a urine volume <0.5 mL/kg regardless of these being consecutive or not.

Patients with no AKI diagnosis by either criterion were compared with patients diagnosed exclusively by the urine output criterion, exclusively by serum creatinine criterion and by both criteria. We compared the demographics and risk factors for AKI in these groups of patients. We assessed the rate of progression to more severe stages of AKI, need for RRT, length of ICU stay and ICU mortality in these patients by AKI diagnosis.

Statistical analyses

Continuous variables were expressed as mean±SD and analysed by unpaired Student's *t*-test or Wilcoxon rank-sum test, as appropriate. Nonparametric variables were expressed as median and 25th–75th percentiles, and analysed by Mann–Whitney's test. Categorical variables were expressed as absolute (*n*) and relative (%) frequency, and were analysed by Pearson's two-test or Fisher's exact test, as appropriate. All statistical tests were two-sided, and $P<0.05$ was considered significant. Statistical analyses were conducted using SPSS 17.0 (Chicago, IL, USA).

Results

Incidence of oliguria

Seventy-five patients were included in this study; the mean time of follow-up was 48 h (IQR 48–96 h). Forty-one (55%) patients presented with an episode of oliguria (UO1–4) during their ICU stay. Using the total urine volume over a 6-h period (UO2 and UO3), more patients were classified as oliguric than by the AKIN definition of AKI that requires six consecutive hours with <0.5 mL/kg (UO1) (Table 1). Of 41 patients classified by UO2, 22 had persistent oliguria (<6 mL/kg over a 12-h period), further classified as UO4 (AKIN stage 2).

AKI diagnosis

Twenty-one (28%) patients were diagnosed as having AKI based on the serum creatinine criteria, whereas urine output criteria identified 41 (55%) patients with AKI (Figure 1). Four patients classified by the serum creatinine criteria did not develop oliguria. Of 41 patients classified by the UO (1–3) criteria, 24 were not classified by the serum creatinine criterion.

Table 2 compares the demographic and patient characteristics at ICU admission among patients with no AKI, AKI exclusively by sCr, exclusively by UO and by both criteria. There was no difference in the number of CKD patients or reference serum creatinine among the groups. The cumulative fluid balance for the entire ICU stay was significantly different among the groups, with the greatest fluid accumulation in patients meeting both criteria.

Outcomes by AKI diagnostic criteria

Of 17 patients diagnosed by both criteria, nine (53%) reached UO stage 2 criteria (UO4) and four (23%) serum creatinine stage 2 criteria (Figure 1). Of patients diagnosed as AKI exclusively by urine output criteria, 15 (62%) progressed to AKIN urine output stage 2 criteria (Figure 1). Five patients (6%) were dialyzed, and three patients started dialysis before reaching any of the AKI diagnosis criteria.

The overall mortality rate was 15% and varied in each group (Table 2). Patients with AKI diagnosis exclusively

Table 1. Urine output definitions

	UO	Number of patients (%)	Definition
Stage 1	1[a]	37 (50)	UO <0.5 mL/kg/h for at least 6 consecutive hours
	2	41 (54)	UO <3 mL/kg during any 6-h period
	3	40 (53)	UO <3 mL/kg during a 6-h fixed block (e.g. 6AM–12PM)
Stage 2	4	24 (32)	UO <6 mL/kg during a 12-h block

UO, urine output.
[a]The definition in RIFLE [7] and AKIN [10] criteria for AKI was considered the standard definition.

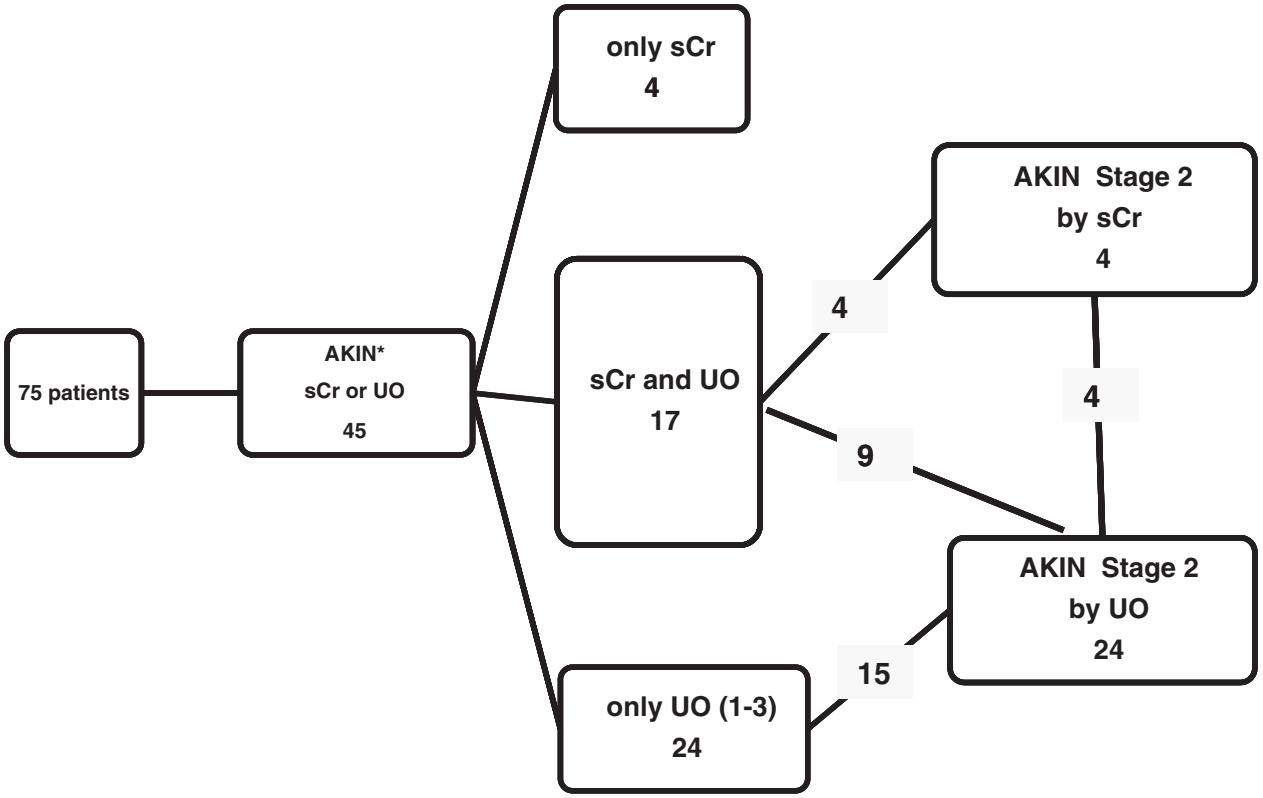

Fig. 1. Patient classification by AKIN classification system. Applying (asterisk) the actual serum criteria defined by the AKIN classification system (AKIN), and any of the proposed urine output definitions.

by UO criterion (1–3) had a non-significant higher mortality than non-AKI patients (17% AKI exclusively by UO vs. 7% non-AKI; P=0.50). However, patients with prolonged oliguria, reaching UO4, had a significantly higher mortality rate than non-oliguric patients (non-AKI 7% vs. 33% AKI by UO4; P=0.004).

Hours of oliguria and number of episodes of oliguria in survivors and non-survivors

The median number of hours of oliguria among all patients was 14 (IQR 4–27). Non-survivors presented more hours with a urine volume <0.5 mL/kg [non-survivors median 29 (IQR 24–84) vs. 12 (IQR 2–23) in survivors; P=0.004]. In AKI patients, there was an increment in mortality rate in patients who had 12 h or more of oliguria (Figure 2A). In those patients who did not meet AKI criteria, 15 patients had >6 h with urine volume <0.5 mL/kg. Of these 15 patients, only one patient died who had a total of 7 h of oliguria. Among oliguric patients (UO3), the median number of oliguria episodes was 5 (IQR 2–12). Patients with more than three episodes of oliguria presented a significantly higher mortality rate—30% vs. 6% in those with less than three episodes of oliguria (P=0.010) (Figure 2B).

Discussion

The traditional way of monitoring urine output by visual readings of the amount of urine accumulated in a urine metre is often inaccurate and with a frequency providing limited data to clinicians. The AKIN and RIFLE classification systems recognized the need to include urine output measurement in smaller time intervals. The AKIN system classifies as stage 1 of AKI (corresponding as RIFLE 'R') patients with a urine volume <0.5 mL/kg/h for at least six consecutive hours [7–10]; however, this criterion is often difficult to implement as they require accurate hourly measurements of urine output. As a result of the difficulties in measuring and recording hourly urine volume, a few studies have validated the AKIN urine output criterion. In studies that compared urine output and serum creatinine criteria, the urine output criterion was often modified, and the period of observation to apply the criterion was limited (Table 3).

Although other studies have demonstrated increased sensitivity of the urine output criterion to diagnose AKI, the specificity of this criterion has not been defined yet [3,4,11–13]. Joannidis *et al.* [13] analysed data from 16 784 ICU patients in the SAPS 3 database. In that study, urine volume was assessed in a 24-h interval, and the AKIN UO criterion was modified, classifying patients with <0.5 mL/kg/h in 24 h as RIFLE I. Although using a less sensitive UO criterion, they classified 14% more patients as AKI than if they had used sCr criterion only. They showed that patients with AKI defined by the worst modified UO criterion in the first 48 h of ICU had increased mortality in comparison to non-AKI patients. In our study, we were able to classify 50% more patients as AKI applying both urine output and serum creatinine criteria, and AKI patients by any oliguria definition had longer ICU

Table 2. Demographic and patients characteristics, and outcomes

	No AKI *n*=30 (40%)	AKI by any UO definition (no sCr) *n* = 24 (32%)	AKI by sCr only *n*=4 (5%)	AKI by UO and sCr *n* = 17 (23%)
Demographics				
Age (years)	55 ± 15	61 ± 13	64±7	69 ± 15*
Weight (kg)	76 ± 29	78 ± 22	93 ± 27	75 ± 11
Race				
Caucasian	23 (76)	21 (87)	4 (100)	15 (88)
African American	3 (10)	1 (4.2)	0	1 (5)
Gender (male)	16 (57)	12 (50)	3 (75)	10 (58)
Co-morbidities				
CKD	3 (10)	2 (8.7)	0	2 (12)
Reference sCr (mg/dL)	0.95 (0.87–1.4)	0.9 (0.8–1.57)	1.2 (0.72–2.05)	1.1 (0.8–1.35)
Hypertension	11 (36)	13 (54)	4 (100)	12 (70)**
DM	6 (20)	4 (17)	1 (25)	5 (30)
Chronic heart failure	10 (33)	3 (12)	2 (50)	3 (17)
Chronic liver disease	4 (13)	7 (30)	0	6 (35)
Chronic lung disease	9 (30)	6 (25)	4 (100)	2 (11)***
Fluid balance				
Daily intake (L)	1.6 (1.3–2.5)	2.4 (1.5–3.1)	2.0 (1.7–2.3)	2.5 (1.6–3.5)
Median daily fluid balance (L)	−0.3 (−1.0–0.3)	0.1 (0.6–1.2)	−0.9 (−1.5– −0.2)	0.5 (−0.1–1.7)
Cumulative fluid balance (L)	−0.1 (−0.8–1.4)	0.7 (−1.7–3.5)	−1.0 (−6.3– −0.1)	3.0 (0.5–1.2)^*
Sepsis	4 (14)	5 (20)	1 (25)	8 (47)^^
Progression of AKI stage				
UO stage 2	0	15 (62)	0	9 (53)
sCr stage 2		0	0	4 (23)[a]
Outcomes				
Need for dialysis	3 (10)[a]	1 (4)	0	1 (6)
sCr at ICU discharge	0.9 (0.8–1.3)	0.9 (0.6–1.2)	1.1 (1.0–2.4)	1.4 (0.9–2.8)^^^
Length of ICU stay (days)	1 (1–2)	1 (1–3)	2 (1–4.5)	4 (1–6)
sCr at hospital discharge	0.9 (0.8–1.2)	1.0 (0.6–1.2)	1.2 (0.9–2.3)	0.9 (0.6–1.9)
Length of hospital stay (days)	7 (2–11)	4.5 (1–7)	7 (3–13)	8 (6–12)
Hospital mortality	2 (7)	4 (17)	0	5 (30)

sCr, serum creatinine in milligram per decilitre; UO, urine output.
Difference for groups: *P=0.057; **P=0.031; ***P=0.005; ^*P=0.008; ^^P=0.094; ^^^P=0.091.
[a]Three patients started dialysis before reaching any of the AKI diagnosis criteria.

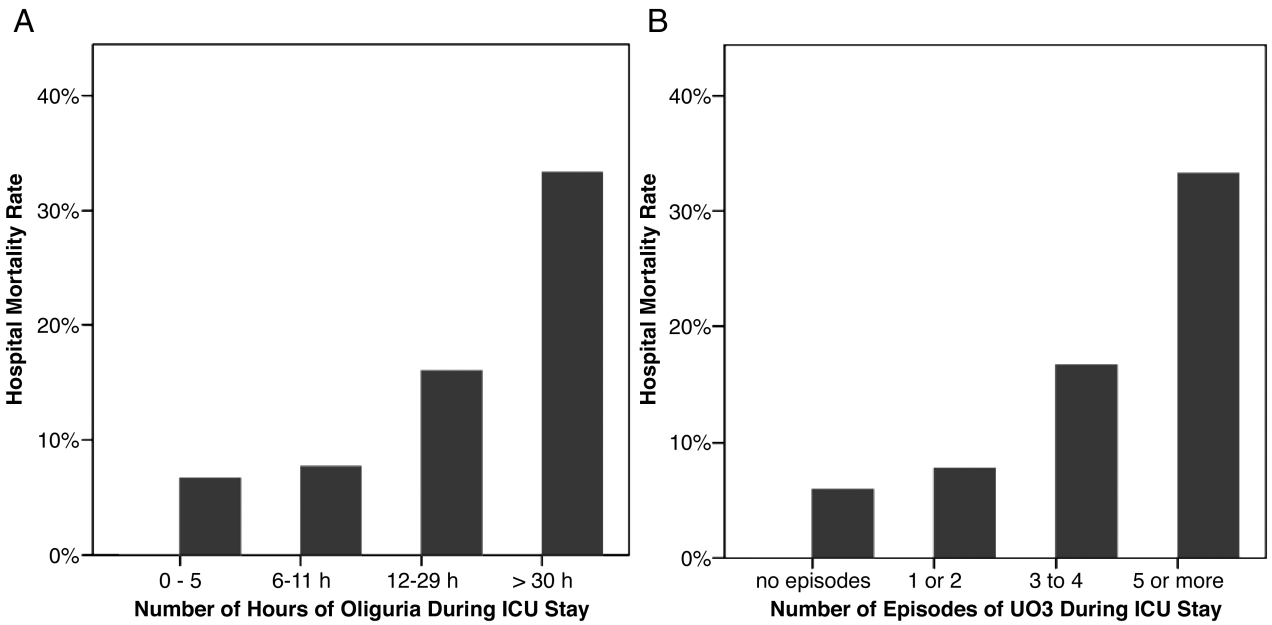

Fig. 2. A. and **B.** Mortality rate by number of hours and number of episodes of oliguria during ICU stay. Difference for groups: A. P=0.176, B. P= 0.046.

Table 3. Studies applying the urine output and serum creatinine criteria in ICU patients

Author	Year	*n* (total)	AKI patients	UO criteria used	Period of observation
Abosaif [1]	2005	NA	183	RIFLE criteria	First day of ICU admission
Cruz [14]	2006	2164	234	RIFLE criteria	ICU stay
Hoste [4]	2006	5383	3617	RIFLE criteria (urine volume at least once every 2 h)	Hospital stay
Kuitunen [16]	2006	813	156	RIFLE criteria	During cardiac surgical intensive care unit stay.
Akcan-Arikan [17]	2007	150	123	PRIFLE criteria	Up to 14 days
Barrantes [18]	2008	471	213	AKIN criteria	ICU stay
Haase [11]	2009	282	127 (AKIN) 130 (RIFLE)	AKIN criteria	sCr criterion within 7 days post-operatively and urine output criterion during ICU stay.
Joannidis [13]	2009	16784	11 003 (7.2%) AKIN 5093 (35.5%) RIFLE	UO <0.5 mL/kg/h to AKIN stage 2 or RIFLE injury	First 48 h of ICU admission.
Morgan [19]	2010	2379	228 patients (9.6%) met the RIFLE class F AKI criteria.	Urine output <0.3 mL/kg/h for 24 h or anuric for 12 h	ICU stay

stay and a higher risk of mortality in comparison to non-oliguric patients (Table 2).

Studies applying both urine output and serum creatinine criteria have shown discordant effects in the AKI-associated mortality by adding the UO to sCr criterion. In a study by Cruz and colleagues, the multivariable analysis showed that RIFLE classes had the best predictive ability for mortality when using the serum creatinine and urine output criteria associated [14]. Haase *et al.* [11] analysed the outcome of patients classified exclusively by UO. The UO criterion applied in the first 48 h showed a lower predictive value for in-hospital mortality compared with the sCr criterion. In a systematic review [3], the relative risk for death among studies that used both creatinine and urine output criteria was lower than in those using the creatinine criterion only. In our study, need for dialysis was more frequent, length of ICU stay longer and mortality rate higher in patients exclusively diagnosed by UO criteria in comparison with patients without AKI. We demonstrated that applying the UO criteria, in addition to the sCr, increases the ability of the AKIN classification to predict mortality; the area under the ROC curve increased from 0.60 when applying only the sCr criterion to 0.65 including UO and sCr. The worst outcomes were found in patients with oliguria and serum creatinine changes, perhaps representing higher severity of illness. We also showed that the number of hours of oliguria and the number of episodes of UO3 are associated with increment in mortality rate, demonstrating the relevance of repetitive episodes of oliguria during ICU stay.

While UO can be considered a marker of renal function and a criterion that correlates with outcomes, devices providing a continuous and accurate measurement of urine flow are not widely available. Although the changes in urine flow can be a result of external influences, such as drug administration, and not a reflection of the GFR, true declines in renal function could be detected earlier with more frequent observations of the parameter. The hourly information on urine volume provides an opportunity to treat urine flow as a continuous physiological variable, instead of as an interval parameter, providing more time points for the detection of AKI. For intervention trials or prevention and treatment of AKI, accurate hourly monitoring of urine flow and volume would provide more time points for intervention [15]. On the other hand, for retrospective evaluations and prospective epidemiologic studies of AKI, the assessment of total urine volume in a longer time interval could facilitate the application of the criteria, since most hospitals do not have digital monitors to record UO hourly. Balancing the practicality of using longer time intervals against ascertaining urine flow every hour to diagnose oliguria is challenging. In our study, we addressed these issues by evaluating the incidence of oliguria based on various definitions, and compared the sensitivity and specificity of these definitions using the sCr AKIN criterion as the gold standard. UO1 and UO2 intend to compare the hourly measurement of urine volume to the total volume in a 6-h time interval. The assessment of UO3 in a fixed 6-h interval intended to evaluate if applying the criterion in blocks of 6 h matching nurse's shift would decrease its sensitivity. We demonstrated that assessing the urine volume in a 6-h interval (UO2–3) resulted in an increased sensitivity as compared with UO1, in which the urine volume has to be <0.5 mL/kg every hour during six consecutive hours (Figure 3). Additionally, our finding that the duration of oliguria was significant only in patients who met the AKI criteria, i.e. had a minimum of six consecutive hours with low UO, highlights the importance of a minimum time interval of 6 h for defining AKI.

While our prospective study provides important information on urine flow characteristics in an incident ICU population, it also has several limitations. Patients were only seen in one medical ICU, and details of fluid type and concomitant medications were not recorded. The main limitation of this study is that data regarding the severity of illness were not available, and we could not determine this difference between the three groups of AKI patients (diagnosed exclusively by UO only vs. exclusively by sCr vs. by both UO and SCr). Secondly, whether volume status in these patients was optimized first, prior to applying definitions of oliguria to diagnose AKI, could not be assessed.

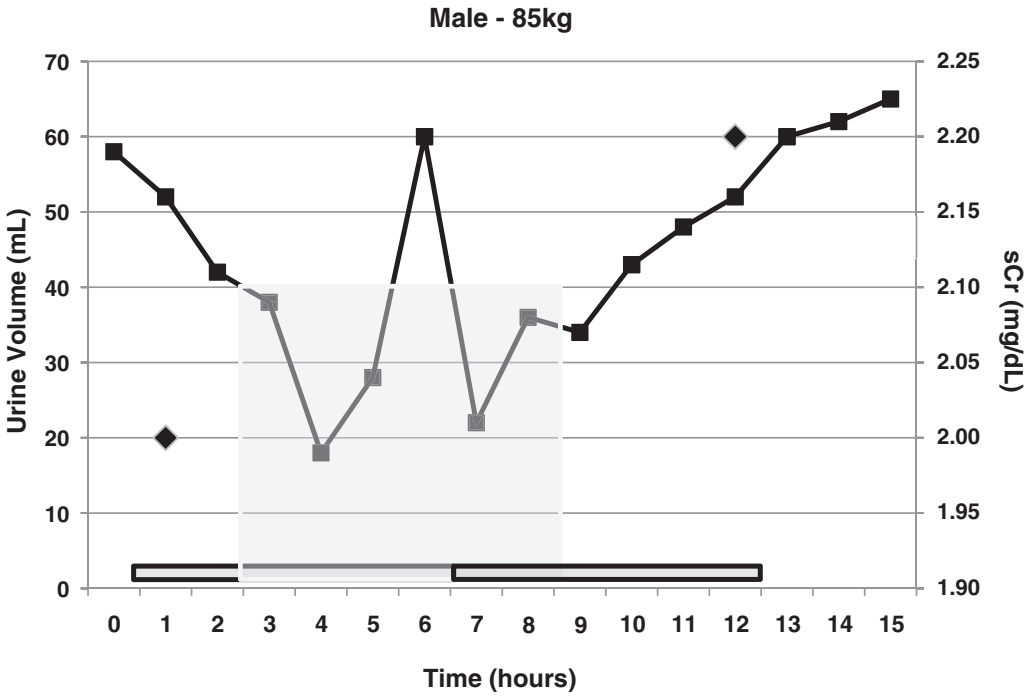

Fig. 3. Urine volume and serum creatinine of a patient classified by the urine output 2 definition but not classified by definitions 1 or 3. An 85-kg patient would be classified as AKI by the UO2 definition [urine volume <3 mL/kg in six consecutive hours (first bar in the timeline)], however, would not be classified by UO1 (<0.5 mL/kg every hour for six consecutive hours) as there was 1 h with a urine volume >0.5 mL/kg/h. Similarly, the UO3 definition was not met since the urine volume was >3 mL/kg in the predefined UO3 6-h interval (second bar in the timeline). Urine flow (squares); serum creatinine (diamonds).

Thirdly, we used, as the reference serum creatinine, the first sCr measured at ICU admission; as some patients may already had elevated serum creatinine at the time of admission, this fact could have lowered the number of patients diagnosed exclusively by the sCr criteria. Finally, we recognize that the sample size is small considering the great heterogenicity of a medical ICU population. Nevertheless, our findings of a high incidence of urine output changes in this population and relationship to adverse outcomes amplify the need for additional studies in larger cohorts.

Conclusions

Real-time and accurate monitoring of urine output could improve the clinical management of patients in the ICU, and enable clinicians to early recognition of kidney injury. Identification of decreased urine output can be achieved by utilizing a fixed time block-based assessment with no significant decrease in the sensitivity to identify AKI patients. Urine output appears to be a valid criterion with prognostic value in patients with AKI. Additional studies are needed to validate these findings and further dissect the implications of oliguria episodes.

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Conflict of interest statement. None declared.

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Application of the RIFLE criteria in patients with crush-related acute kidney injury after mass disasters

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Abstract

Background. The term acute kidney injury (AKI) and its classification in strata defined as Risk, Injury, Failure, Loss and End-stage renal failure (RIFLE) need to be validated in different patient groups. RIFLE may be useful to foresee medical and logistic problems in crush-related AKI in disaster victims.

Methods. Taken from the Marmara earthquake crush database, the subjects included 416 patients who were categorized according to the modified RIFLE criteria and 18 victims with crush injury but with normal serum creatinine who served as controls. Associations between each RIFLE category and various parameters were investigated.

Results. There were 27, 79 and 310 patients in the risk, injury and failure groups, respectively. Urine volume and serum albumin were lower; blood pressure, blood urea nitrogen, serum uric acid, potassium and phosphorus were higher; oliguric and polyuric periods were longer; medical complications were more frequent; and number of transfusions, dialysis sessions and days of dialysis support were higher in more severe AKI categories. Glomerular filtration rate at discharge was progressively lower in proportion to the severity of RIFLE classification. However, survival outcome did not differ among controls and patients who suffered from AKI nor in between RIFLE categories.

Conclusions. In disaster crush victims, RIFLE classification can be useful to foresee the medical complications, need for therapeutic interventions and logistic support and also renal function at discharge though, perhaps, not survival.

Keywords: acute kidney injury; crush syndrome; rhabdomyolysis; RIFLE

Introduction

Traditionally, acute renal failure (ARF) has been defined as an ‘abrupt and sustained decrease in renal function resulting in retention of nitrogenous and non-nitrogenous waste products’ [1]. However, this vague terminology does